

**WO 01/12252 A1**

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## Injection Means

5 This invention relates to improvements in devices for delivery of substances such as drugs, vaccines, fluorescent or magnetic material, and dyes into a surface, such as the skin of a human being, animal or other organic matter. The substance may be a solution, particulate fluid, or a paste, for example.

10 Numerous such apparatus have been proposed in the past. A simple hypodermic syringe is the most well known although other mechanical arrangements, such as an auto-injector which are manually operated are well known.

Also mechanically operated apparatus have been proposed to facilitate injections and this enables higher speed of injections to be achieved which can reduce the pain of the injection and consequent bruising, bleeding etc.

15 US Patent 5681283 discloses the use of a system in which needles are injected into the skin using elastic bands at a high velocity with the intention of making the injection "painless" and US Patent 5564436 discloses a pneumatically operated automatic rotating cassette with a plurality of stylets so that the higher velocity can  
20 reduce the pain of the injection.

We have now devised an improved apparatus and method for injecting substances into a surface which facilitates the use of higher speeds.

25 According to the invention there is provided apparatus for injecting a substance into a surface which apparatus comprises a needle, a container for the substance to be injected, a means for applying the substance from the container to the tip of the needle, a means for driving the needle to penetrate the surface and deliver the substance thereto which means comprises a block slidably mounted in a conduit

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which block is accelerated by a controlled force to strike the needle assembly thereby inducing an acceleration of the needle to drive it into the surface.

5 Preferably there is a connection between the needle and the container which has sufficient flexibility to allow the needle to penetrate the skin without the connection being broken.

10 In existing hypodermic syringes and other apparatus the needle is directly attached to the container for the substance being injected and the needle and container move as one unit so the needle penetrates the surface.

15 However when a higher velocity of injection is used sufficient force must be applied to accelerate the needle plus container plus substance being injected to the desired velocity and to stop them, either by the frictional resistance to the injection by the surface or by a stop mechanism and the greater the mass, the greater the forces and energy required and the more likelihood of pain, bruising, bleeding etc. when the needle penetrates. In addition the greater the mass the more robust and heavy the driving means must be and the greater the noise in operation, greater wear etc.

20 The present invention minimises the driven mass and so reduces or overcomes these problems.

25 If the mass of the fluid to be injected is sufficiently low the reservoir for the fluid can be incorporated with the needle so that the needle and reservoir are accelerated as one unit, the volume of fluid should be less than 1ml e.g. mass of fluid should be less than 1 gram.

30 Preferably the needle holder mass (together with fluid reservoir if included) i.e. the mass of the needle and associated moving parts is 0.01 to 5.0gram, more preferably 0.1 to 3grms and most preferably 0.2 to 0.6gram., with a typical mass being about

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0.6grms., this also means that the needle and other connected components have less kinetic energy and this reduces the risk of bruising etc. This is different to other techniques of injection, such as the injection of animals with tranquillising darts, when the needle penetrates the surface and forms part of, or is rigidly connected  
5 directly to a chamber containing the substance to be injected.

Preferably the mass of the block is from 0.8 to 3 times the needle holder mass and more preferably from one to twice the mass.

10 The present invention enables very high acceleration of the needle to be attained and the acceleration of the needle is preferably 1 to 20,000g.

Under these conditions of high acceleration and/or high velocity it is important that the needle moves very straight along its axis and any lateral or transaxial movement  
15 or flex is kept to a minimum. In one embodiment of this invention the block is made to move very straight along its axis and to strike the needle assembly squarely and centrally. Also the needle assembly preferably includes a guide to restrict lateral or transaxial movement and this also minimises flex.

20 The needle driving means may include one or more of a leaf spring and stop arrangement, or a bistable spring or diaphragm arrangement. The needle driving means may include a mechanically hydraulic, pneumatic or electromechanically driven drive mechanism.

25 A preferred driving means is pneumatically operated and comprises a block slidably mounted in a conduit so that application of a pneumatic force at one end of the conduit generates a pulse of gas e.g. air which will propel the block at speed down the conduit, so that it will strike a end piece, which is connected to the end of the needle. Preferably the block can be returned to its original position by reduction of

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pressure in the conduit. In this way one or more pulsed impulses can be applied to the end piece with the block being withdrawn back down the conduit between pulses.

5 Preferably the block is positioned in contact with the source which generates the pulse of air so that the end of the block acts as a seal and is held in position with air pressure built up behind the block. When a release mechanism is operated the block is free to move and is propelled by the air pressure down the conduit. A preferred seal is for the end of the block to have a tapered shape and to fit into a corresponding shape at the end of tube connected to the pneumatic source so that the end of the  
10 block forms a tight seal. The end of the block acts as a plug valve and can form a tight fit and is held in position by frictional forces. To operate, the block is given a small push or nudge to overcome the frictional forces, whereupon the block moves down the conduit. The device can be primed ready for use with the block in place and air pressure built up behind the block ready for release.

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The end piece which is struck can be the end of the needle suitably reinforced if need be, or it can be an end piece or the like attached to or forming part of the needle. The end piece will normally have a flat end which is struck for ease of operation although this is not essential

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Suitable means for applying the pneumatic force include hand held bellows, pre-compressed gas, a piston with a spring return or a motorised means. The bellows can, for example be in the form of a sealed rubber chamber connected to the conduit. Another means of operating is by means of a pen injector which can be conveniently  
25 carried and used as required.

There can be a source of compressed gas which generates a pulse of gas and this compressed gas can be a gas such as carbon dioxide or air etc. The pneumatic force can also be generated by the generation of a gas by the evaporation of a liquid such as

water or an organic liquid e.g. by an electrical heater so the gas formed propels the block down the conduit.

5 In another embodiment there is a reduction of pressure in the conduit below the block in the direction the block moves i.e. so that a partial vacuum is formed and this reduction in pressure propels the block. The block is then "sucked" down the conduit.

This method using a reduction in pressure can be used on its own or in conjunction with the application of pneumatic force as described above, either sequentially or  
10 simultaneously.

In a preferred embodiment of the invention there is provided a means whereby the needle is driven into the skin in steps by contacting the skin with the needle, applying a blow to the needle e.g. as described above so that the needle penetrates a controlled  
15 distance into the skin and then optionally applying another blow or blows to the needle to drive the needle in to the desired depth.

For example the needle can be driven into the skin until it is in contact with bone and then a blow is applied to the needle to drive it into the bone e.g. to inject into the  
20 bone marrow. The mass of the shuttle and needle holder should be sufficient to drive the needle through the bone to the required depth.

If a plurality of blows are required this can be carried out as described above and/or there can be two or more blocks slidably mounted within the conduit so that a plurality  
25 of blows impact on the end piece.

Alternatively the needle and block can be slidably connected together and spaced apart so that they are propelled down the conduit together and, when the needle enters the skin and stops, the block continues and strikes the end of the needle so that there

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is a double hit i.e. when the needle strikes and enters the skin and then when the block strikes the end of the needle and drives it further in.

5 In another embodiment, a valve and port arrangement, known to those skilled in pneumatics, used with compressed gas drives the block towards the needle assembly. When the block reaches the end of its travel, the valves exhaust the forward driving pressure and apply pressure in the reverse direction to the block. The reciprocating cycle is then repeated as often as required.

10 In another embodiment part of the momentum of the moving block can be transferred to the syringe plunger to induce pressure which injects a quantity of the substance to be injected into the skin.

15 If a rapid series of injections are required e.g. in which the needle penetrates only a small distance into the skin, a motorised means can be used to generate the pulse of air and subsequent reversal of pressure.

20 In one embodiment of the invention the substance to be injected is contained in a reservoir fluidically connected to the needle and there are means to accelerate the needle independently without accelerating the reservoir. This means that there is less mass to be accelerated so it is easier to accelerate and to stop the needle.

25 The feed of the substance to the needle can be discontinuous and synchronised to the time when the needle is beneath the skin so that a series of small volumes of the substance can be injected into the patient.

30 The needle can be separate and adjacent to a syringe containing the substance to be delivered with one end of the needle flexibly connected to the end of the syringe by for example a flexible tube or by a coiled length of the needle so that rapid movement of the needle is not significantly inhibited by connection to the syringe. The

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needle is driven by the driving means until it has penetrated to the required depth and then the syringe is operated to inject the substance contained in the syringe through the needle into the surface.

- 5 In another embodiment a syringe has a piston operating in the normal way with the needle projecting through the end of the syringe and the needle having an extension projecting through the piston so the end of the extension can be struck by a driving means to drive the needle into a surface, there being a connection means between the syringe and the needle whereby the substance in the syringe can pass through the
- 10 needle from the syringe as the piston is depressed. In use the needle is placed against the surface and the end of the extension is struck as referred to above to drive the needle into the surface and then, when it has been driven into the required depth, the piston is depressed to inject the substance in the syringe into the surface.
- 15 Preferably the needle is driven into the skin of the user by applying one or more impacts to the end of the needle to drive the needle into the skin to the desired depth and then the substance to be delivered is applied through the needle.

- Optionally there can be a needle guide which can fit around the needle to assist in the
- 20 location and positioning of the needle and keeps the needle exactly on line during the injection and reduces any risk of the needle bending. In addition the guide can help guard against needle stick injury when the needle is withdrawn and can serve as a depth control.

- 25 It is a feature of the invention that the mass which has to be accelerated to high velocities is much less than in other techniques which enables low energy to be used to propel the needle and makes it much easier to stop. It enables very high accelerations e.g. 1 to 20,000 g to be easily achieved by simple means. For example the pneumatic pressure required can be obtained by blowing down the conduit.



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It has been found that the needles used can be blunter and it has been found that, for at least some applications, a blunter needle i.e. one which has a rounded or conical tip and which has no, or less sharp, cutting surfaces compared to a typical hypodermic needle or lancet can be used and this structure can cause less cutting of capillaries and bleeding. This is thought to be due to the blunter needle, when driven at the speeds of the present invention, forces the components of the skin such as capillaries, cells etc. apart rather than cutting them as would be done with sharper needles. This reduces the risk and incidence of bruising and the possible formation of fibroids and the like. For some people such as haemophiliacs this is a great advantage.

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This advantage was surprising and contrary to what would otherwise be thought as it is difficult, painful and causes tissue damage to penetrate skin with a blunt needle unless the skin has been pre-cut.

15 Preferably the needle is hollow with at least one aperture connecting to core directly adjacent to the tip to allow injections to be made at a depth optionally of less than 1mm below the skin surface. The needle can have a substantially non-cutting tip with substantially no sharpened edges or blades with smooth, tapered, radiused or bevelled edges or surfaces.

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Alternatively the needle can be conical or with a radiused point and one or more slots are present which connect the core to the exterior to allow, in use, delivery of the substance below skin surface and in which, when the needle is entering the skin, the one or more slots are substantially closed to prevent entry of external material or tissue into the core and when fluidic pressure is applied from the core to the exterior dimensions of the one or more slots increases to allow greater flow of fluidic substance.

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The one or more slots can be linear and parallel to the needle axis, inclined at an angle to the axis, spiral in form or are arranged to define a moveable flap which

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closes like a valve when external pressure is applied to the needle and opens like a valve when internal pressure is applied.

5 The present invention is particularly useful for use with high speed injection methods for example when the needle has a velocity of 1 metre per second to 100 metres per second in order to penetrate the skin and deliver the substance thereto.

10 Preferably the driving means drives the needle at a velocity of at 5 to 50 metres per sec, more preferably 6 to 35 metres per sec., or 10 to 20 metres per sec. e.g. 15 metres per sec.

15 For persons who have to have frequent injections such as diabetics, who need to inject insulin on a regular basis, the reduction of bruising, bleeding etc. is also a great advantage and the present invention is particularly applicable for use with such people.

20 After injection the needle can then be withdrawn from the surface and it has been found that, in at least some applications, a relatively slow withdrawal of the needle can reduce the risk of bruising to the skin.

In other applications, needle withdrawal is improved by a rapid reverse acceleration of the needle, and this can be achieved by release of a compressed spring or reverse action of the moving block for example.

25 There can be a connection between the needle and the block so that as the block is withdrawn the needle is withdrawn from the surface into which it was injected. This feature is particularly useful in applications such as injecting through a finger nail when, with conventional syringes the needle can be jammed in the nail and can be difficult to remove e.g. pliers have to be used to pull the needle out.

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As well as for use in injecting fluids the apparatus of the present invention can also be used to aspirate.

The invention is illustrated by example in the following non limiting examples.

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#### Example

A tube and pneumatic drive was used to accelerate a block at 0.4g to a velocity of 5 – 15 metres per sec. To strike a radius tip 28 gauge needle assembly weighing 0.2g  
10 adjacent to the skin. The needle contained a lateral hole adjacent to the tip and was driven 10mm into the skin of the arm with no pain, was able to deliver a small quantity of sterile saline to the skin and left no blood or bruising on withdrawal.

For comparison an injection device was tested which fired a 29 gauge bevel tip  
15 hypodermic needle at 4 metres per sec. into the skin of the arm to a depth of 11mm. There was significant pain, some bleeding after withdrawal of the needle and bruising developed around the penetration site taking 5 days to disappear.

The invention is described in the accompanying drawings in which  
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Fig. 1 is one embodiment of the invention and  
Fig. 2 is another embodiment of the invention

Referring to Figure 1 a syringe (10) has a piston (1) mounted within it which can be  
25 depressed by handle (2). There is an outlet (4) from the syringe so that, when piston (1) is depressed, a substance in the body of the syringe (3) is forced out through the outlet (4). Attached to the outlet by a Luer connector (5) is one end of needle (13). The needle (13) is flexible and fixed to a holder (6) the needle can be a zig-zag shape or it can be coiled as shown in figs. 1a and 1b. Attached to holder (6) is a striker plate  
30 (8) which is the end piece to needle (13) and is slidably mounted within conduit (9),

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there is block (20) positioned in the conduit. The end A of the conduit (9) is connected to pneumatic pump or the like so that air under pressure can enter the conduit and propel the block (20) down the conduit to strike plate (8). Reversal of the direction of the air in the conduit will cause the block (20) to be sucked back to the end of the conduit.

In use the substance to be injected is placed in the syringe (10) and the one or more blocks (20) are at the end of conduit (9) remote from the end of the needle (7). The end of the needle (7) is placed against the surface to be injected and a pulse of high pressure air is sent down conduit (9) so as to propel the one or more block (20), at the required high speed i.e. above 1 metre per sec, down conduit (9) to strike plate (8). The needle is then driven into the surface and an impact made on the plate (8) and the needle penetrates the surface. When the needle has penetrated the surface the piston (1) in the syringe (10) is depressed and the substance in the syringe is injected into the surface.

Referring to Figure 2 a syringe (24) has a needle (27) attached to one end and the needle has one or more openings near the tip (27) outside the syringe end seal (31) and the needle has further openings along shaft (23) lying inside the syringe end seal whereby a substance in the syringe can enter the needle. An extension (28) to the needle (27) passes slidably and sealably through the piston (25) and terminates in a striker plate (29). The striker plate is positioned in conduit (30) down which blocks can be propelled pneumatically to strike plate (29).

In use the syringe is filled with the substance to be injected and the needle (27) is placed against the surface, a block or blocks are propelled down conduit (30) in a similar way to that described for Figure 1 and striker plate (29) and so drive the needle into the surface. When the needle has penetrated the surface to the required depth the piston (25) is depressed and the substance injected into the surface.

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It will be appreciated that all of the embodiments of the present invention can be arranged to deliver many different substances into skin. The substance may be a traditional tattoo dye, a temporary dye, a drug, a gene therapy substance, a particulate substance, for example.

## Claims

1. Apparatus for injecting a substance into a surface which apparatus comprises a needle, a container for the substance to be injected, a means for applying the substance from the container to the tip of the needle, a means for driving the needle to penetrate the surface and deliver the substance thereto which means comprises a block slidably mounted in a conduit which block is accelerated by a controlled force to strike the needle assembly thereby inducing an acceleration of the needle to drive it into the surface.
2. An apparatus as claimed in claim 1 in which, in use, the majority of the energy for penetration after contact with the surface comes from the momentum of the needle and associated moving parts and not from the continued force of the driving means.
3. Apparatus as claimed in any one of claims 1 or 2 in which the driving means is pneumatically operated.
4. An apparatus as claimed in any one of claims 1 to 3 in which there is a stopping means incorporated in the driving means adapted to bring the needle to a rapid stop
5. Apparatus as claimed in claim 4 in which the driving means comprises a block slidably mounted in a conduit so that application of a pneumatic force or spring at one end of the conduit will propel the block at speed down the conduit, so that it will strike an end piece which forms part of, or is connected to the end of the needle.
6. Apparatus as claimed in claim 6 in which there are means to generate a pulse of gas in the conduit which propels the block down the conduit.
7. Apparatus as claimed in claim 5 or 6 in which the end of the block is tapered and fits into the end of a corresponding shaped tube connected to a source of compressed

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air so as to form a plug valve at the end of the tube, there being means to move the block away from the end of the tube.

5 8. Apparatus as claimed in claim 6 or 7 in which there are means to return the block to its original position by reduction of pressure in the conduit.

9. Apparatus as claimed in claim 8 in which there are means to apply a plurality of pulsed impulses to the plate and means to withdraw the block back down the conduit between pulses.

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10. Apparatus as claimed in claim 9 or 10 in which the block and needle are connected so that as the block is returned to its original position or withdrawn down the conduit the needle is withdrawn from the surface.

15 11. Apparatus as claimed in any one of claims 3 to 10 in which the means to propel the block down the conduit comprises hand bellows, a piston and return spring or a pre-compressed gas or motor driven gas pump.

12. Apparatus as claimed in any one of claims 3 to 10 in which there is a means to  
20 reduce the pressure in the conduit below the block in the direction the block moves so that a partial vacuum is formed.

13. Apparatus as claimed in any one of claims 4 to 12 in which there is provided a means to apply a plurality of blows to the needle so that the needle penetrates a  
25 controlled distance into the skin at each blow until the needle is driven in to the desired depth.

14. Apparatus as claimed in claim 13 in which there are two or more blocks mounted within the conduit so that, in use, a plurality of blows impact on the end piece.

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15. Apparatus as claimed in claim 13 in which the needle and block are slidably connected together and spaced apart so that they are propelled down the conduit together and, when the needle enters the skin and stops, the block continues and strikes the end of the needle.

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16. Apparatus as claimed in any one of the preceding claims in which the feed of the substance to the needle is discontinuous.

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17. Apparatus as claimed in any one of the preceding claims in which the needle is separate and adjacent to a syringe containing the substance to be injected with one end of the needle fluidically and flexibly connected to the end of the syringe and there being sufficient flexibility in this connection so that rapid acceleration and movement of the needle is not significantly inhibited by its connection to the syringe.

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18. Apparatus as claimed in claim 17 in which the needle is coiled, looped or zig-zagged.

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19. Apparatus as claimed in any one of the preceding claims in which there is a syringe which has a piston mounted therein with the needle projecting through the end of the syringe and the other end of the needle having an extension projecting through the piston so the end of the extension can be struck by a driving means to drive the needle into a surface, there being a connection means between and the needle whereby a substance in the syringe can pass through the needle from the syringe as the piston is depressed.

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20. Apparatus as claimed in any one of claims 16 to 19 in which part of the momentum of the moving block can be transferred to the syringe plunger to induce pressure which injects a quantity of the substance to be injected into the skin.



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21. Apparatus as claimed in any one of the preceding claims in which there is a needle guide through which the needle can slide in use to restrict transaxial or lateral movement of the needle.

5 22. An apparatus as claimed in claim 21 in which the needle guide restricts the transaxial or lateral movement of the needle to below  $\pm 2$  degrees.

23. An apparatus as claimed in claim 22 in which the needle guide restricts the transaxial or lateral movement of the needle to below  $\pm 0.5$  degrees.

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24. An apparatus as claimed in claim 21 in which the needle guide restricts the transaxial or lateral movement of the needle to below  $\pm 0.1$  degree.

15 25. Apparatus as claimed in any one of the preceding claims in which there are means, in use, to drive the needle at a velocity of from 1 metre per second to 100 metres per second in order to penetrate the skin and deliver the substance thereto.

26. An apparatus according to claim 25, wherein the needle driving means, in use, drives the needle at a velocity in the range of 5 to 50 metres per sec.

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27. An apparatus according to claim 25, wherein the needle driving means drives the needle at a velocity in the range of 10 to 20 metres per sec.

25 28. An apparatus as claimed in any one of the preceding claims in which the means for driving the needle, in use can accelerate the needle at 1 to 20,000g

29. An apparatus as claimed in any one of the preceding claims in which the mass of the fluid to be injected is below 1 gram and the container for the fluid is incorporated with the needle.

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30 . An apparatus as claimed in any one of the preceding claims in which the mass of the needle and associated moving parts is 0.01 to 5.0gm.

5 31. An apparatus as claimed in any one of the preceding claims in which the mass of the needle and associated moving parts is 0.1 to 3grms.

32. An apparatus as claimed in any one of the preceding claims in which the mass of the needle and associated moving parts is 0.2 to 0.6gm.

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33. An apparatus as claimed in any one of the preceding claims in which the mass of the block 0.8 to 3 times the needle holder mass.

15 34. An apparatus as claimed in claim 33 in which the mass of the block is from one to twice the needle holder mass.

36. Apparatus as claimed in any one of the preceding claims in which the substance to be delivered is fed under normal, manual or mechanical pressure to the needle by means of a syringe or a compressible sack.

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37. Apparatus as claimed in any one of the preceding claims in which there are means to repeat the cycle of needle entry, substance delivery, needle withdrawal.

25 38. Apparatus as claimed in claim 37 in which the rate of injections from 1 to 50 per second.

39. Apparatus as claimed in any one of the preceding claims in which the needle is hollow with at least one aperture connecting to core directly adjacent to the tip to allow injections to be made at a depth of less than 1mm below the skin surface.

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40. An apparatus as claimed in any one of the preceding claims in which the needle has substantially non-cutting tip with substantially no sharpened edges or blades with smooth, tapered, radiused or bevelled edges or surfaces.

5 41. Apparatus as claimed in any one of the preceding claims in which the needle is conical or with a radiused point and one or more slots are present which connect the core to the exterior to allow, in use, delivery of the substance below skin surface and in which when the needle is entering the skin the one or more slots are substantially closed to prevent entry of external material or tissue into the core.

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42. Apparatus as claimed in claim 41 in which when fluidic pressure is applied from the core to the exterior and the dimensions of the one or more slots increases to allow greater flow of fluidic substance.

15 43. Apparatus as claimed in claim 41 in which the one or more slots are linear and parallel to the needle axis, inclined at an angle to the axis, spiral in form or are arranged to define a moveable flap which closes like a valve when external pressure is applied to the needle and opens like a valve when internal pressure is applied.

20 44. Apparatus for injecting a substance into a surface as hereinbefore described with reference to the drawings.

45. A method of delivering a substance by employing an apparatus according to any of the preceding claims.

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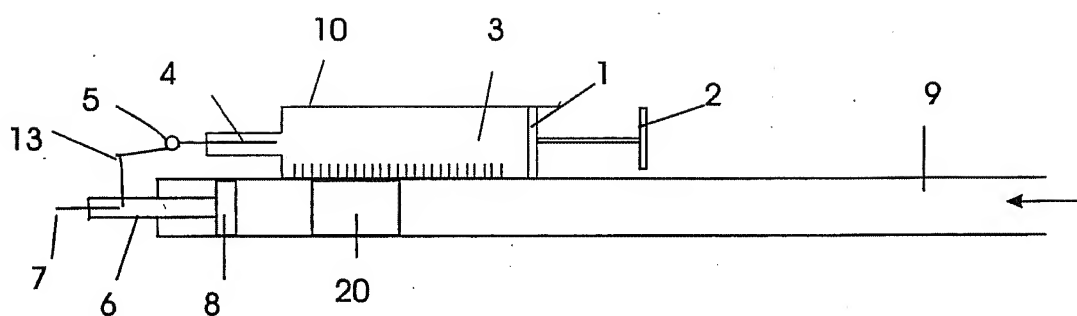


Fig. 1

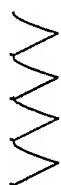


Fig. 1a



Fig. 1b

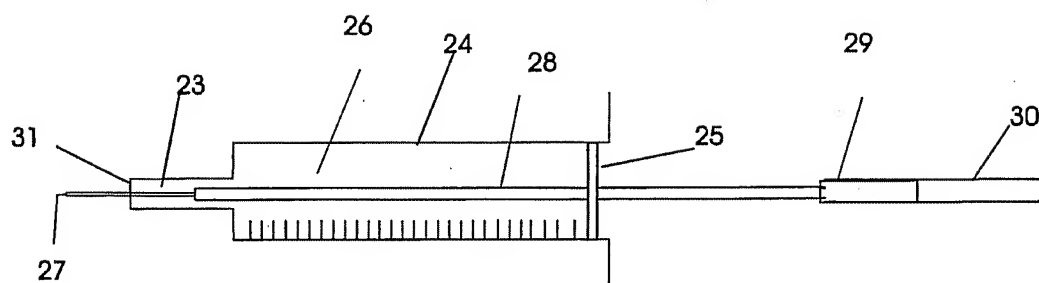


Fig. 2

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 00/03061

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61M5/20 A61M5/42 A61M5/46 A61M5/32

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61M

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	WO 00 09184 A (IMPRINT PHARM LTD ;CROCKER PETER JOHN (GB)) 24 February 2000 (2000-02-24)  the whole document	1-9, 11-14, 17-32, 36,37,40
X	FR 1 215 970 A (P. MUSSARD) 21 April 1960 (1960-04-21) the whole document	1,11,17, 18,36
X	CH 328 609 A (DUNMIRE RUSSELL P) 15 March 1958 (1958-03-15) page 5, line 81 -page 7, line 91; figures 7-11	1,19,20, 36
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Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

\* Special categories of cited documents :

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Date of the actual completion of the international search

13 October 2000

Date of mailing of the international search report

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Name and mailing address of the ISA

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# INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 00/03061

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 92 20388 A (MEDIMECH INT LTD) 26 November 1992 (1992-11-26) abstract; figure 1 page 7, line 4 - line 33 ---	1, 19, 20, 36
A	DE 34 05 671 A (SANDOZ AG) 22 August 1985 (1985-08-22) page 18, line 22 - line 29; figures 1-4 ---	1, 25-27
A	WO 95 29720 A (PA CONSULTING SERVICES ;REVELL WILLIAM JAMES (GB)) 9 November 1995 (1995-11-09) abstract; figure 1 -----	1

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 00/03061

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